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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,222	08/07/2001	Wendi V. Rodrigueza	10173-073	3425

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	14

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/924,222	Rodrigueza
Examiner	**Art Unit**
Gollamudi Kishore	1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 27, 2003* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *17-43* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *17-43* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 13
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The request for the extension of time and amendment dated 3-27-03 are acknowledged.

Claims 1-16 have been canceled and claims 21-47 have been added by applicant. These new claims have been renumbered as 17-43 in accordance to rule 126.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 17-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

According to claim 17, the standard deviation is 30 nm for 68 % of the liposomes. That means the sizes vary from 95 nm to 155. However, according to the dependent claim 18, the mean diameter is between 100-150. This is confusing. If the majority of the liposomes (68 %) have 100-150 sizes, it is unclear how one can get the liposomal sizes with the standard deviation recited in the parent claim.

Double Patenting

3. **The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).**

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The double patenting rejections as set forth in the previous office action and now applicable to claims 17-43 are maintained in abeyance since applicant expresses the willingness to file the terminal disclaimers.

Claim Rejections - 35 U.S.C. § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 30 and 32-36 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 470 437 of record.

EP teaches unilamellar liposomes containing phosphatidylcholine for the treatment of atherosclerosis (note page 7; also columns 5-7 of its English Equivalent, US. 5,556,637). Mechanism by which the composition acts has no significance.

Claim Rejections - 35 U.S.C. § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

6. Claims 17-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP cited above.

As pointed out above, EP teaches the use of empty liposomes of different diameters for the treatment of atherosclerosis. EP does not provide specific examples for the treatment of atherosclerosis. It would however, been obvious to an artisan to use liposomes for the treatment of atherosclerosis based on the teachings of EP. Although in Example 3 where the liposomes of claimed sizes are prepared, the reference indicates the attachment of a DNA marker to the liposomes, it is deemed obvious to one of ordinary skill in the art not to attach the marker if the desired goal is only to treat atherosclerosis in humans and not for diagnostic purposes since the reference through examples shows how to make the liposomes of different sizes. EP does not also specifically teach instant protocol of administration. In the absence of showing unexpected results, these parameters are deemed to be obvious parameters manipulated by an artisan to obtain the best possible results.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Hager does not teach at least 68 % of the liposomes have a mean diameter of 125 +30 nm. This argument is not found to be persuasive since 'at least 68 % indicates that the value can be between 68 and 100 and the reference teaches 129 nm in example 3; applicant has not shown that this value does not fall within the claimed

range. With regard to the Gaussian distribution argued by applicant, the examiner points out that instant claims do not recite this limitation. With regard to applicant's arguments that the DNA marker, propidium iodide in Example 3 of Hager, the examiner points out again that one of ordinary skill in the art will not to attach the marker if the desired goal is only to treat atherosclerosis in humans and not for diagnostic purposes since the reference through examples shows how to make the liposomes of different sizes. The examiner also points out that many DNA alkylating agents are toxic and by themselves are mutagenic and carcinogenic and yet they are used in cancer therapy in humans (The molecular basis of cancer is cited in this context; note pages 262-283). With regard to the unexpected results argued, the examiner points out that the claims.

7. Claims 17-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (BBA, 875, pp., 183-194, 1986) by itself or in combination with EP cited above.

Williams teaches a method of administration of liposomes and liposomes together with plasma (contains lipoproteins) and the alterations in lipid metabolism and the regression of experimental atherosclerosis as a result of such an administration (note the Materials and Methods section and the discussion). What is lacking in Williams is the teachings of the sizes of liposomes. However, the methodology disclosed on pages 184 and 185 indicated that sonicated liposomes were passed through a 0.22 microns filter and therefore, it would have been obvious to one of ordinary skill in the art that the liposomes

would contain liposomes of instant sizes. Even assuming that the sizes in Williams are different from instant sizes, one of ordinary skill in the art would be motivated to use liposomes larger than 50 nm with a reasonable expectation of success since EP which deals with the treatment of same disease state advocates the use of liposomes of instant sizes.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Williams also does not suggest using a population of liposomes falling within the claimed Gaussian distribution. This argument is not found to be persuasive since as pointed out above, instant claims do not recite this limitation. With regard to applicant's arguments that Williams shows that increase in LDL after the administration of SUVs and applicant points out to Fig. 2A of Williams in this regard. A close examination of this figure appear to indicate that even the corresponding controls have the same peak height and therefore, the examiner is unable to determine whether there is a statistically significant difference between values for the controls and the liposomes. Irrespective of this, the rejection is based on the combination and EP teaches instant sizes.

The examiner will allow claims 17-29 (applicant's numbered claims 21-33) provided 1) terminal disclaimers are filed; 2) the limitation that the liposomes are 'empty liposomes' and the limitation that the mean diameters recited have the Gaussian distribution profile are recited in claim 17. That the independent claim specify that the liposomes are empty liposomes was suggested by the examiner during the interview.

8. **Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).**

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

May 30, 2003